Di-n-octylphthalate

CAS #117-84-0
Swiss CD-1 mice, at 1.25, 2.50, and 5.00% in feed
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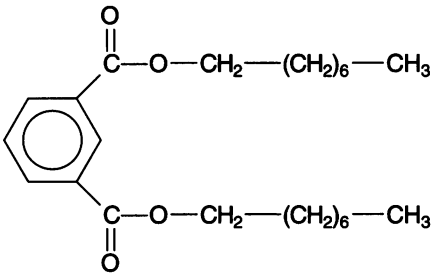

Di-n-octylphthalate (DOP) was tested using the RACB protocol in Swiss CD-1 mice as part of a structure–activity evaluation of a variety of phthalates (Heindel et al., Fundam Appl Toxicol 12:508–518 [1989]). Body weights, food and water consumptions, and clinical signs in a dose-range-finding study were used to set doses for the main study of 0.0, 1.25, 2.5, and 5% in feed. Feed consumption was unchanged by DOP addition. Based on measured consumption, these concentrations of DOP produced calculated consumption estimates of approximately 1.8, 3.6, and 7.5 g DOP/kg body weight/day.

Three controls and two middle dose mice died during the continuous breeding phase. Both treated and contol mice gained an average of 12 to 14% of their original body weight. There was no effect of DOP exposure on the number of litters per pair, the mean number of live pups per litter (control value, 11.5 ± 0.4 pups), proportion born alive, live pup weight adjusted for litter size (control, 1.60 ± 0.01 g) or days to deliver each litter.

In the absence of any demonstrable reproductive toxicity, a Task 3 crossover mating was not performed, and the fertility of the second generation was evaluated for the controls and high dose groups.

In the F_1 mice, growth and viability were unaffected by DOP consumption. Reproduction was also unaffected: the same proportion of treated and control mice mated and bore live litters. The size and viability of these litters was also unaffected by DOP (11.5 pups per litter, controls), as was adjusted pup weight (1.50 ± 0.03 g).

The F_1 adults were killed and necropsied after the F_2 litters were delivered and evaluated. In F_1 females, body weight was unaffected by 5% DOP exposure, but when adjusted for body weight, both liver weight and kidney weight was increased by 22 and 10%, respectively. Treated male terminal body weight was also unchanged by DOP, while adjusted liver weight was increased by 28%, and seminal vesicle weight was decreased by 12%. Epididymal sperm concentration and motility were unchanged by DOP exposure at 5%; the proportion of morphologically abnormal forms was reduced in the treated mice, from a control value of 5% abnormal to 3.5% abnormal in the DOP-exposed males. Estrous cycle length and stage distribution (the proportion of time spent in each estrous stage) was unchanged by DOP exposure.

The single finding of a slight reduction in F_1 seminal vesicle weight is interesting in light of current concerns about second-generational reproductive toxicity but needs confirmation. Overall, these data show that at doses that induced significant hepatomegaly di-n-octylphthalate was without any adverse reproductive effect in Swiss CD-1 mice.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB85218147**
Chemical: **Di-n-octylphthalate**
CAS#: **117-84-0**
Mode of exposure: **Feed**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	1.25%	2.5%	5.0%
General toxicity	Male, female	Male, female	Male, female
Body weight	—, —	—, —	—, —
Kidney weight[a]	•	•	•
Liver weight[a]	•	•	•
Mortality	—, —	—, —	—, —
Feed consumption	—, —	—, —	—, —
Water consumption	•	•	•
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
$\bar{x}$ litters/pair	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	—, —
Cumulative days to litter	—	—	—
Absolute testis, epididymis weight[a]	•	•	•
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	•
Epidid. sperm parameters (#, motility, morphology)	•	•	•
Estrous cycle length	•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	•	•

F_1 generation — Dose concentration →	1.25%	2.5%	5.0%
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	•	•	—, —
Mortality	•	•	—, —
Adult body weight	•	•	—, —
Kidney weight[a]	•	•	—, ↑
Liver weight[a]	•	•	↑, ↑
Feed consumption	•	•	—, —
Water consumption	•	•	•
Clinical signs	•	•	•
Reproductive toxicity			
Fertility index	•	•	—
# live pups/litter; pup wt./litter	•	•	—, —
Absolute testis, epididymis weight[a]	•	•	—, —
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	—, ↓
Epidid. sperm parameters (#, motility, morphology)	•	•	—, —, ↓
Estrous cycle length	•	•	—

Summary information	
Affected sex?	Both, unclear
Study confounders:	None
NOAEL reproductive toxicity:	5.0%
NOAEL general toxicity:	Unknown
F_1 more sensitive than F_0?	No
Postnatal toxicity:	No

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); —, —, no change in males or females. [a]Adjusted for body weight.